NSLS-II Beamline Development Proposal

Type I [X] Type II [ ]

Flexible Access and Highly Automated Beamline for Macromolecular Crystallography - AMX

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A. Science Case

X-ray crystallography has transformed our understanding of biological processes. It was X-ray diffraction that provided the first clues to the structure of the DNA double helix nearly 60 years ago, giving profound insights into how DNA is replicated. One of the major driving forces in the continuing development of synchrotron radiation facilities worldwide has been the reality that knowledge of biological structure imparts deep insights into the mechanism of action of molecules and assemblies, and that the difficulty in determining those structures increases as they get larger.

Seven recent Nobel Prize winners in Chemistry depended on readily available synchrotron X-rays for their ground-breaking research: Sir John Walker of the MRC in 1997, Roderick MacKinnon of Rockefeller University in 2003, Roger Kornberg of Stanford University in 2006, Roger Tsien of the University of California San Diego in 2008, Venkatraman Ramakrishnan of the MRC, Thomas Steitz of Yale University, and Ada Yonath of the Weizman Institute of Science in 2009. The ribosome structures, honored with the 2009 Nobel Prize, are the largest with 150,000 atoms. Determination of this structure – the location of every atom! – was an amazing *tour de force*. These recent awards help prove the crucial role synchrotron radiation facilities continue to play in extending our understanding of the mechanisms of life.

The routine use of synchrotron radiation for single crystal diffraction studies has revolutionized macromolecular structural biology. With the availability of brighter X-ray sources, the size and complexity of macromolecules that can be studied has increased by an order of magnitude. Advancements observed for the past 15 years in the development of cloning, expression, purification, and crystallization methods have been impressive. However, crystals of the most complex structures that are suitable for diffraction are often scarce and difficult to obtain. Therefore, continuing advances in synchrotron radiation sources, detectors, and software are required to tackle the most challenging problems, which are the ones most likely to make a significant impact on our knowledge of the functioning of living systems.

Structure determination by synchrotron crystallographic methods has long evolved from a physicist's specialty to a readily available method for the molecular biologist, the cell biologists, and the academic and industrial investigator in the medical and pharmacological disciplines. This dynamic continues today as biologists rapidly expand their investigation of molecular function to include entire biochemical pathways. Macromolecules emerge as dynamic structures responding to signals, as switches, sensors, or movers, and others that carry out biochemical reactions or are part of higher order molecular machines. Often, intermediate states can be stabilized by chemically constructed substrate analogues, by genetic or biophysical manipulation and thus become amenable to structure determination of one frame in the movie of a molecular transition. Frequently, insights gained from crystallography are just a piece in the puzzle that may also require direct imaging, solution scattering, computational biology and other complementary methods to assemble a more complete rendering and understanding of a cellular process.

These themes, the exacting structure determination of large macromolecular complexes, and the determination of large numbers of structural variants of macromolecules, including drug binding studies, are detailed by many investigators that wrote in support of this beamline development proposal. The AMX beamline must support them all.

AMX Mission: The AMX beamline at NSLS-II will provide investigators with a highly accessible facility, featuring both automated and remote participation as well as rapid personal access. It will fully exploit the remarkable source brightness of the new light source across a broad energy range. It will support current and emerging styles of data collection and structure solving and it will have the capacity and flexibility to accommodate new ones made possible by its speed and versatility. We anticipate that the facility will accomplish these objectives:

- Begin operation at 'first light' to provide continuity for ongoing NSLS user programs
- Support programs that require testing of vast numbers of specimens (*e.g.* membrane proteins)
- Support crystallographically difficult projects (*e.g.* large unit cells, choice of energies)
- Operate at throughput rates that can replace screening by data collection on every specimen
- Support asynchronous data collections for multiple simultaneously proceeding projects
- Provide assistance and technology to facilitate remote operation from home institutions
- Offer crystallographic decision making by near real-time software assistance
- Support *in-situ* optical absorption spectroscopy

AMX is part of the MX Suite: To provide best-in-class experimental facilities for all macromolecular crystallography problems, we intend to develop specialized instruments, integrated into a comprehensive suite. Table 1 reveals the six beamlines that the NSLS MX community plans for the first few years of NSLS operation. Each will fill a unique niche in our overall plan to provide advanced capabilities for regional, national, and international scientists. The absence of any one will leave us with unmet needs.

Table 1. Proposed suite of MX beamlines.

FMX	Frontier micro-focusing MX at an undulator	Tunable, 1 to 100 μm beams, preservation of coherence, diverse crystal-manipulation apparatus and automated specimen delivery
AMX	Flexible access highly automated MX at an undulator	Tunable, 5 to 300 μm beams, automated specimen delivery, remote operation and participation, convenient access for experimenters
AM3	Flexible access MX at a 3PW	Tunable, 25 to 300 μm beams, crystal screening automation, convenient access for experimenters
SMX	Coordinated MX and optical spectroscopy at an undulator	Tunable, 5 to 300 μm beams, spectroscopies to include absorption, fluorescence, Raman and IR vibrational; automation for crystal mounting, integrated data collection
SM3	Coordinated MX and optical spectroscopy at a 3PW	Tunable, 25 to 300 μm beams, spectroscopies to include absorption, fluorescence, Raman and IR vibrational; and XAS/EXAFS, automated specimen handling
NYX	NYSBC microdiffraction at an Undulator	Novel high-energy-resolution monochromator produces 5 to 50 μm beams, accurate goniometer, pixel-array detector

The AMX beamline will complement the FMX micro-focusing beamline, proposed separately. Each will have a specialized mission on an undulator source, but with significant overlap of experimental capabilities. The crystallographer who puts a premium on the efficient high quality data collection from his challenging but quite tractable crystalline systems will take advantage of the AMX instrument, and others who require micro-diffraction capabilities to extract structural information from truly small or heterogeneous crystals will choose the FMX beamline. Locating both stations on a pair of canted undulators in one low-β straight section emphasizes the continuity between them, and the synergy resulting from shared access protocols, support staff, computing resources, and ancillary equipment. A conceptual floor layout of the AMX - FMX pair of beamlines is shown in Figure 1.

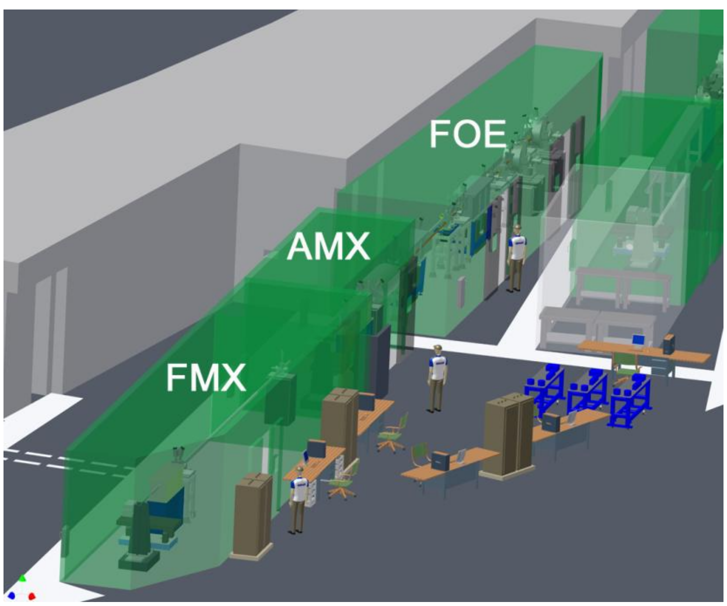


Figure 1. View of the conceptual layout of the AMX and FMX beamlines on a pair of canted undulators. The first optical enclosure (FOE) serves both stations. The AMX hutch is in the center of the figure and will be wider than shown, and the FMX station will extend further down-stream. Portions of the SM3 combined MX and optical spectroscopy or the AM3 flexible access station are shown in the top right corner.

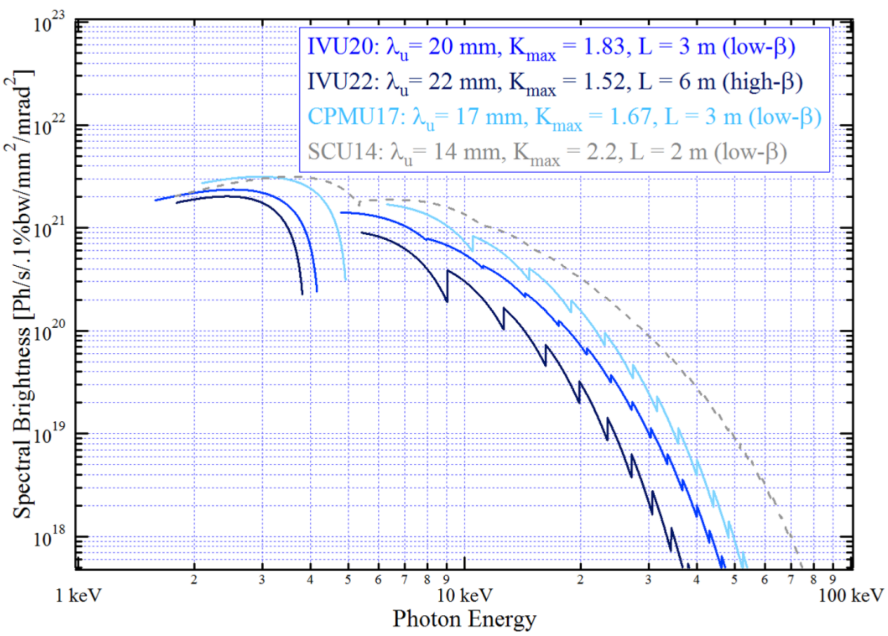
This MX beamline, AMX, will fully exploit the high brightness and collimation qualities of NSLS-II, and will provide unprecedented access to users, so its presence is critical to achieving NSLS-II mission goals.

B. Beamline Concept & Feasibility

X-ray source:

To accomplish its mission, we plan for the AMX beamline to have a tunable energy from 5 to 25 keV and feature a simple optical layout with a beam spot size varying from 5 µm to a defocused beam of 300 µm. Whereas the fine focus overlaps with the FMX capabilities and meets the needs of crystallographers working with small specimens or a desire to sample parts of larger ones, the full-sized beams serve those investigating larger crystals to get the full benefit of crystal volume in providing precise data. To obtain beams smaller than the native focus one must trim the source size thereby losing precious flux. We combat this by placing the AMX beamline on the highest brightness source available. Additionally, high brightness allows one to produce low divergence beams. This is important for data collection on large molecular complexes that invariably have large unit cells and typically require a beam divergence < 200 µrad to achieve good separation of Bragg diffraction spots.

Choice of undulator: The NSLS-II Conceptual Design Report (CDR) identifies the brightest source as the U20 permanent magnet in-vacuum undulator sited in a low-β straight section. Figure 2 shows its spectral brightness and essential parameters along with those of the U22 and the future cryogenic permanent magnet (CPMU17) and the superconducting (SCU14) undulators. Clearly, the superconducting SCU14 undulator, a concept beyond today's technology, would be the optimal choice, providing the highest brightness and a near continuous spectrum from 1.8 to 50 keV.



U20	
Photon energy range [keV]	1.9 – 30
Type of straight section	Low-β
Total device length [m]	3
Period length [mm]	20
Number of periods	148
Minimum gap [mm]	5
Peak magnetic field [T]	1.03
Kmax in linear mode	1.83
Minimum fundamental [keV]	1.6

Figure 2. Calculated spectral brightnesses of planned NSLS-II insertion devices are plotted as a function of photon energy. That of the U20 is the 2nd line from the bottom (blue). From Oleg Tchoubar and NSLS-II CDR.

Of the two fully developed in-vacuum undulators, the 3 meter long U20 is the device of choice because it is designed for low-β straights and short enough to be deployed in canted pairs in the 6.6 meter long straight section. By contrast, the 6 meter long U22 device of similar performance is designed for use in high-β straights. As shown in Figure 2, the U20 has a remarkably smooth spectrum that will greatly help to make energy and heat load changes equally smooth. Its gap between the fundamental and higher harmonic emissions is narrow and extends from 4.2 keV to 4.8 keV. Anomalous diffraction measurements at the absorption edges of iodine and xenon, the two biologically relevant elements in that range, will then be handicapped by a flux deficit of an order of magnitude.

X-ray optics:

Two specialized MX beamlines: The AMX proposal for a highly automated MX station assumes that the FMX micro-focusing beamline will complement its specialized capabilities. We plan that the two stations will exploit a pair of canted undulators in a common low-β straight section. The AMX beamline, the shorter of the two, will occupy the outboard ray coming from the upstream undulator, and the FMX beamline, extending to the periphery of the experimental floor, will occupy the inboard ray derived from the downstream undulator. While the AMX optical layout is optimized to conserve brightness and therefore uses a one-stage beam focusing scheme, the companion micro-focusing beamline is optimized to achieve a small beam spot with a two-stage focusing scheme. The optical concept of the AMX beamline is given in Figure 3.

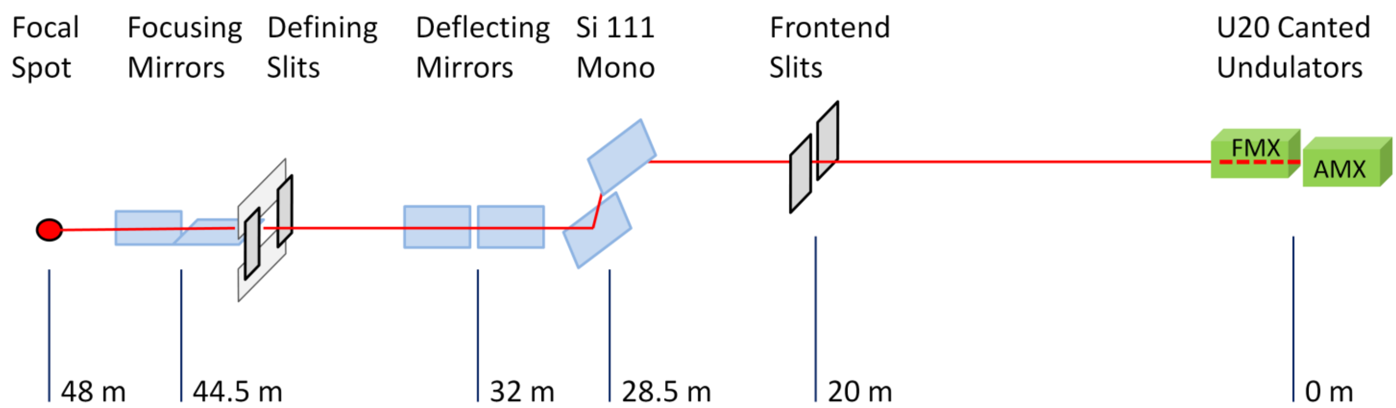


Figure 3: Optical concept of the AMX beamline.

Canting: The first challenge is to achieve sufficient lateral separation between the two beam paths such that the AMX instrument can accommodate a large area detector, in spite of the beam pipe traversing its hutch to the downstream station. We will achieve it with a variation of the GM/CA-CAT design, employing canted undulators and side-deflecting mirrors. The NSLS-II CDR states that undulator cant angles of 1 mrad are acceptable. The angle between a pair of white beams is then 2 mrad. At the point where they emerge from the ring wall at 25 meters from the center of the straight section they will have a lateral separation of just 50 mm.

Monochromator: Double-crystal monochromators are the first optical elements on each of the paired beamlines. They will employ flat silicon (111) crystals. The first crystal will be cooled by flowing liquid nitrogen which, according to the finite element heat transfer analysis described in the NSLS-II CDR is sufficient to keep lattice distortions small compared to the Darwin width of the crystals and thus not degrade energy resolution. However, the expected thermal bulge will add a slope error of about 6 μrad RMS and blur the beam dimension and divergence accordingly. This significant effect exceeds that of best available mirrors by a factor five and will be compensated with adjustable downstream vertical focusing elements. A second important function of the pair of monochromators is to separate the two canted beams vertically by a few cm. The monochromator in the FMX branch will be the leading device and deliver its beam at a high elevation. Just downstream, the AMX monochromator will deliver its beam at a lower horizon.

Side-deflecting mirrors: With this accomplished, one can achieve substantial lateral separation of the canted beams through the use of tandem pairs of horizontally-deflecting mirrors installed in each beamline. The first pair of deflecting mirrors intercepts the lower outboard AMX beam and performs two consecutive reflections of a beam incident at 4 mrad on each mirror, imparting a total outboard deflection of 16 mrad. The second pair of deflecting mirrors acts on the upper inboard FMX beam, deflecting it inboard by 16 mrad, and focusing it towards the beamlines' virtual source point. The total angular separation of the two beams is then 34 mrad and the lateral separation of the beam centerlines at the sample location in the AMX hutch becomes 44 cm. This is sufficient to accommodate an experimental station complete with a large area detector. Provided that the mirrors have very small figure errors of 1-2 μrad, their contribution to beam divergence will be tolerable.

Focusing: The active optical elements of the proposed AMX beamline are listed in Table 2 extending from the undulator source to the specimen position at 48 m. That distance, which underlies the conceptual layout discussed here, may increase by several meters if this beamline were located on a sector with the extended floor space made available by the recently announced introduction of bypass walkways at the building's periphery.

Device	*Distance from U20*	*Beam Size hxv [μm]*
In-vacuum U20 Undulator	0 m	77 x 14
Front-end Slits	~ 20 m	900 x 350
Double-crystal Monochromator	28.5 m	1280 x 500
Horizontally Deflecting Mirrors	32 m	1440 x 560
Beam-defining Aperture	42.5 m	1910 x 740
Vertically Focusing Mirror (demag = 11:1)	44 m	1980 x 770
Horizontally Focusing Mirror (demag = 15:1)	45 m	2020 x 580
Sample Axis	48 m	5 x 1

Table 2. Active optical elements in the AMX beamline, their distance from the exit of the U20 undulator, and beam cross sections assuming mirrors with 0.1 μrad RMS slope error.

The electron beam source dimensions and opening angles in a low-β straight section are 77 μm (h) x 14 μm (v) and 45 μrad (h) x 7.5 μrad (v) respectively (all values FWHM). For the photon beam, the source dimensions are similar, except that the finite energy spread of the electron beam in a U20 increases the vertical opening angle of the photon beam to about 17.5 μrad (for a photon energy of 12 keV).

Achieving a vertical focus size of a few μm in the experimental AMX hutch should not pose a great difficulty for the beamline optical system. Perfect focusing optics employing a demagnification factor of 14:1 would suffice in the vertical direction to yield a 1 μm line. However, because residual slope errors of the vertical focusing mirror may dominate in determining the beam size, it will be located close to the focal position, at 44 m and just 3 m upstream of the specimen axis resulting in a vertical beam size of 2 μm (assuming a mirror slope error of 0.1 μrad). The resulting demagnification factor of 11:1 will increase the native beam divergence only modestly to about 190 μrad, well below the required 1 mrad limit.

Focusing the beam in the horizontal direction to a desired size of ~5 μm is more of a challenge. Several options can be considered. (1) By using only the horizontally focusing mirror at 45 m (see table 2), a demagnification ratio of 15:1 is obtained that – with perfect optics - will focus the native beam to a 6 μm spot and yield an acceptable beam divergence of 680 μrad. For smaller beam widths, we will trim the source width by closing the front-end or the beam-defining slits. This option has the notable advantage that the figure of only one optical element needs to change when the size of the beam spot is adapted to the crystal at hand. (2) Alternatively, we could accomplish horizontal focusing by employing the monochromator's second crystal or even the deflecting mirrors to pre-focus the beam into the final horizontally focusing mirror. This arrangement will make shifting of the focal length and spot size a more complex and slower undertaking. Should this proposal go forward, we will carry out extensive optical studies to find optimal solutions for horizontal beam focusing.

Expected flux: No recent physical optics calculations have been carried out to forecast accurately the flux and intensity expected for the AMX beam line. However, adapting calculations for the flux through the virtual source aperture of the similarly configured (to this intermediate location) FMX beam line and reference to the NSLS-II CDR yields an estimated flux of about 10^{13} ph/s in a 6x2 μm^2 beam of 12 keV.

Beam diagnostics: We will put great emphasis on placing multiple beam diagnostic devices along the beam path such that the beamline will be amenable to implementing real-time auto-alignment methods. Beam position monitors will report beam position and intensity after each major optical element and high-resolution beam profile imaging devices will provide feedback to maintain the x-ray optical alignment during routine operation. Additionally, all moving elements will be equipped with position encoders to preserve long-time stability and to create a rational data base that will support the correlation of optical settings with actual performance in data collection. Furthermore, we plan to insert sufficient slit systems and moveable apertures to facilitate exacting single device alignment with wave-front analysis techniques.

Experimental systems:

Beam conditioning and goniometer: The beam delivery section of the AMX line will be equipped with the customary complement of beam attenuators, fast acting shutter, beam-position monitor, high precision defining slits, in-line video camera for specimen centering and observation, and an array of guard apertures in a shared vacuum enclosure. The specimen goniometer will feature a high precision air-bearing omega spindle with horizontal axis, complete with a three-axis orthogonal specimen-centering stage and topped with a miniature kappa head with phi-spindle. Thus it will be possible to orient crystals along vectors that result in favorable data collections. Their centering will be maintained dynamically by machine-vision systems such as STAC[1]. Movable beam stops of various sizes and a fluorescence counter will complete the setup. To promote stability and to maintain relative alignment, all of this standard equipment will be supported on a common vibration suppressing monolith. Several commercial companies offer highly developed and functional units that integrate all of these devices efficiently.

In-situ optical spectroscopy: We plan to equip the crystal goniometer axis with a sturdy optical system for the measurement of UV and visible light absorption spectra of crystals in the x-ray beam. The light path of this spectrometer will be perpendicular to the beam. Capabilities for more discriminating spectroscopy, sampling the exact volume interrogated by the X-ray beam as well as Raman spectroscopy will be available on the proposed SMX and SM3 beamlines nearby.

Asynchronous data collection: Recognizing the potential for unprecedented data collection speeds and specimen throughput that result from the combination of the very high x-ray flux and fast pixel-array detectors that impose no image readout delay, it is necessary to devise a specimen automounter complement that can keep up with the expected typical rate of one specimen per minute. At these speeds, experimenters will no longer have time to analyze diffraction as it is being collected and contemplate next actions. The experiment will become an asynchronous process where investigators will judge and analyze data that have already been stored away. This leads quite naturally to a new method of allocating beam time to multiple simultaneous users that each get a fraction of the beam time and will have their data collections completed in turn.

Specimen handling systems: We envision a nimble robotic system to support the asynchronous data collection of many queued specimen from a number of simultaneously scheduled projects. At its core are two essentially identical specimen mounting robots, each capable of picking frozen specimen from ‘pucks’, mounting crystals, and retrieving them. The pair will operate in a synchronized way such that as soon as one removes a specimen, the other pops a new one up without the delay that would occur if only one device were active, had to store the retrieved specimen, find the next one, and segue back to the goniometer. A third robot will replenish the supply of pucks and specimens available to the pair of automounters. It will operate through the hutch wall and deliver new pucks from cryogenic storage dewars outside the hutch as well as retrieve pucks that are no longer needed in the hutch. Operator personnel will load its hopper with user’s specimen.

User access to hutch: Of course users and staff may still access the hutch in the traditional way and mount crystals by hand, as may be necessary for special or sensitive crystals or they may want to configure auxiliary apparatus needed in exploratory experiments. However, the fully automated data exchange and data collection will be the main stay of AMX operation controlled by experimenters working from remote workstations in the LOBs, somewhere on site, or at their home institutions.

[1] STAC is a software developed by the European Molecular Biology Laboratory in Grenoble.

Detector: The phenomenal flux expected from a U20 beam makes a complete data collection of say 360 consecutive frames of 1º oscillation angle truly short: perhaps 3.6 s total and 0.01 s per frame. These short exposure times, and the advent of pixel array detector technology make possible a new shutter-less data collection method where the omega spindle advances continuously and the detector framing substitutes for the shutter operation defining each oscillation increment. The currently available commercial detector, the Pilatus 6M, has a maximal framing rate of 12 Hz and a readout dead-time of 3.6 ms. Impressive as these specifications are, the performance is insufficient for use in shutter-less data collections on a non-attenuated NSLS-II beam because 3.6 ms are about a third of 0.01 s, the time of covering 1º. Multiple and staggered angular sweeps will be needed for a complete reciprocal space mapping as required for successful data reduction and structure determination. However, a more desirable solution would be a faster framing detector approaching a kHz or more. Developments in this direction are under way and the fastest of several that may be ready by 2015 should be acquired to make best use of the AMX beams.

Software: To accomplish a high degree of automation in beamline auto-alignment, specimen handling, data-collection methods, multi-user management, and remote participation will require not only an excellent programming staff, but also experience in an integrated environment where software developers interact with scientific staff and users. Our existing Python- and EPICS[2]-based CBASS system will serve well as the overall control software for the beamline. Our programmers are active in expanding data collection methods to pixel-array detectors and advanced database methods. Collaborations with groups at other synchrotrons, for example with programmers from the European consortium that created the STAC mini-kappa software or the EDNA[3] system, will provide software for crystallographic decision making, as well as advanced applications of machine vision and device control.

C. Required Technical Advances

Undulator: Though not a requirement for the success of this proposal and program, we desire to outfit the undulator from the start in such a way, that when need or opportunity arises, we can upgrade it to cryogenic operation. The resulting higher magnetic remanence of its magnets at liquid-nitrogen temperatures would extend the tuning range of individual harmonics towards lower energy, thus narrow the spectral discontinuity between harmonics, yielding even higher brightness. Extrapolating calculations from the NSLS X25 undulator to the U20 device indicates that at the Se K edge on its seventh harmonic the gain in brightness will be more than 50%. Should this proposal go forward, we plan to determine expected gains in brightness due to cryogenic operation of the actual U20 undulator in collaboration with NSLS-II machine physicists.

Cant angle: One would like to have an undulator cant angle larger than the currently prescribed maximum of 2 mrad between the two beam centerlines to provide more elbow room at the specimen location in an upstream hutch traversed by the beam pipe of the downstream one. Should accelerator studies conclude that cant angles twice the current maximum are tolerable, we may also reduce the number of beam deflecting mirrors in the FMX proposal and thus eliminate their contribution to the effective beam divergence.

Mirrors: Mirrors of the highest quality surface finish and the lowest available figure error and roughness are critical for the success of this proposal because these will be used to separate the AMX and FMX beams emanating from a pair of canted U20 undulators. As discussed above, a tandem pair of mirrors will be deployed near the midpoint of each beam line. Thus, mirror imperfections contribute twice to increased beam divergence. Given the width of the native beam at the mirror locations of about 1.5 mm, and the proposed glancing angle of 2-4 mrad, each individual mirror will need to be about 75 cm long.

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[2] EPICS is a mature device control software package developed and maintained at ANL and many other laboratories
[3] EDNA is an data collection software collaborative project of researcher at EMBL, ESRF, CCLRC, MRC-LBM and BNL

Robotics: The fabrication and control of the three specimen handling robots described above, two automounters working in synchrony plus a puck-delivery machine, are an appealing engineering challenge that should best be pursued in close collaboration with established manufacturers of current generation cryogenic specimen handlers. As other beam lines and programs may face similar challenges, these initiatives should be coordinated among interested parties.

Software: We are already developing software for automated crystallographic decision making and data collection, for the transfer and efficient storage of vast amounts of data, for fast and reliable instrument control, for user program interfaces and data bases that are a match to the expected high data collection speeds. Should this proposal be approved, we will pursue this work with vigor and without delay.

D. User Community and Demands

The nine existing MX beamlines at NSLS are an amazing engine for structural biology. In particular, since the beginning of 2005 there have been 2800 PDB submissions and 1795 new publications discovered from the nine active and two legacy* NSLS beamlines: X3-A, X4-A, X4-C, X6-A, X8-C*, X9-A*, X12-B, X12-C, X25, X26-C, and X29. Of the publications, over 10%, 185 were in the premier journals Science, Nature, and Cell. We also observe that X29 is now the second most productive beamline in the world in PDB depositions with 250 in 2009. The highest number is 290 from the BER-funded third-generation undulator 19ID at the APS. No other beamline comes close. Three recent winners of the Nobel Prize in Chemistry, Roderick MacKinnon in 2003, and Venkatraman Ramakrishnan, and Thomas Steitz in 2009, employed beamline X25 and other NSLS beamlines for significant portions of their prize-winning work.

This remarkable productivity is possible for several reasons. An important one is that the NSLS lies within easy driving distance of the productive arc of molecular and structural biologists from Philadelphia to Boston. Many northeastern crystallographers feel they and their groups have an advantage actually to visit NSLS rather than to visit possibly more impressive beamlines in other places. Coming here affords opportunities to pursue synchrotron work on short notice when their needs warrant a day trip. This demand for easy, personal access will help to drive use of NSLS-II beamlines.

A second source of productivity results from the enthusiasm of the local staff for pursuing the very best apparatus and methods. We were using the X25 wiggler for MX by 1999. We constructed the X29 undulator beamline by 2004 and soon implemented effective rapid access protocols that led to today’s multiple users on each day. We installed the X25 undulator in 2007 and have offered microbeams since 2009. Steady operation of cryogenic automounters began by about 2008. The coordinated MX and optical spectroscopy station also began operation on 2008. We will install a fast-framing Pilatus pixel-array detector in 2011. These and many continual advances in the past have kept the attention and supported the productivity of a large user community.

A third and critical reason for the high productivity of NSLS MX beamlines is the strong culture of service within the beamline staff. We pioneered in the early ‘90s the use of the Web for rapid access proposals, and now essentially all of the beamlines are accessible in this way. A comprehensive experiment-tracking database system is coupled to the proposal process. Also available is the transformative and hugely productive Mail-In crystallography program for academic users. Finally we offer a regular series of training opportunities including crystal-growth workshops, the Crystallographer’s Workbench, and the internationally renowned RapiData course, now with nearly 600 alumni. These keep a focus on the NSLS MX beamlines and their capabilities.

A fourth strength of the MX programs at the NSLS is the frequent and long-standing interaction between the greater MX community and our resident staff. In addition to contacts at beamlines, meetings, and courses, all of which yield new ideas and countless suggestions, the MX community is actively involved in long-range planning. These investigators helped to make the scientific case for NSLS-II, and area crystallographers helped define and drive the many workshops that underpin this proposal. We created a chronology of our planning for MX at NSLS-II in Appendix II (page 29), including mention of our interaction with the local community. See also a chronology of selected meetings on the NSLS-II life sciences website: http://www.bnl.gov/nsls2/sciOps/LifeSci/default.asp.

The key characteristics of the AMX beamline of providing rapid and flexible access for multiple simultaneous local and remote users, of streamlining productivity by resorting to a high degree of automation, and of emphasizing data quality by implementing fast and accurate methods of optimizing beam size (3-300 μm) and energy (5-25 keV) will likely benefit a wide range of academic and industry-based investigators. The following scientists have written letters of support for this application and have outlined how AMX will contribute to their current and planned investigations. These letters are compiled in Appendix III (page 31).

The remainder of the proposal, containing personal and financial information, is removed.